EXHIBIT A

light of the ineffectiveness of conventional therapy, and because the disease had progressed to include hip joint involvement, which invariably leads to crippling of a child, this child became a candidate for the combined antibody treatment of the present invention.

As described above, and using immunological, techniques, antibodies to IFNγ ("anti-IFNγ antibodies") and antibodies to TNFα ("anti-TNFα antibodies") were obtained by immunizing goats with r-IFNγ and r-TNFα, respectively, and isolating IgG from the immunized animals. Each milliliter of IgG contained approximately 50 mg of protein, and the antibodies showed a 1:5 signal to noise ratio at 1:12,500 dilutions by ELISA (assays performed by CytoImmune Sciences, Inc., College Park, Md.).

Two (2) ml/day each of anti-IFNγ antibodies (3 days) and anti-TNFα antibodies (5 days) were administered parenterally to the child. By the second week of observation, absence of morning stiffness, elimination of hip joint pain, and considerable increases in the level of physical activity, range of motion in the affected joints, and grip strength were noted (See, Table 3). X-rays of the child showed improvement in the appearance of the femurs and hip joints, and greater delineation of articular spaces. Repeated testing of the child indicated a significant drop in disease activity, as shown by clinical and laboratory parameters, including pain, stiffness, grip strength, C-reactive protein, and others (See, Table 3). The improvement in clinical status and the nearly normal range of motion in the child's hip joints persisted into the fourth month, as shown by x-rays at regular check-ups. After six months (the most recent data available), damage to the child's femurs and acetabulae were less marked as shown on x-rays, and she continued to improve in other parameters, to the point that on the advice of an orthopedist, her joints were allowed to bear greater weight.

TABLE 3

Dynamics of clinical and laboratory parameters in patient with JRA, after treatment with anti-IFNγ antibodies and anti-TNFα antibodies

Parameter	Before Treatment	Week 1	Week 2	Week 3	Week 4
Arthralgia score*	4	2	2	0	0
Joint stiffness (min.)	30	10	0	0	0
Grip strength (mm/Hg)	20	44	72	68	70
Angle of abduction-rt hip (degrees)	15	15	20	n/a	30
Circumference of right wrist (cm)	12.9	12.7	12.2	11.9	12.0
ESR	6	3	8	6	6
C reactive protein (g/l)	0.6	neg	neg	neg	neg

*Scale of 0–5 where 5 is most intense pain
n/a = Not available.

These data point to a role of cytokines in AD, and again reinforce the conclusion that a common pathological mechanism underlies clinically disparate forms of autoimmune disease. It is the differences in the target cells affected that result in the varying clinical manifestations of the autoimmune response in a patient.

As demonstrated by the results produced in this child, neutralization of certain cytokines with antibodies can break the chain of pathological reactions and normalize the synthesis of other induced cytokines in the patient. Other types of autoimmune disease can be treated by the use of anti-cytokines, singly or in combinations, to counteract autoimmune aggression and inflammation. Good results have been reported from double-blind placebo controlled trials using chimeric monoclonal anti-TNFα antibodies to treat RA (Elliott et al., *Lancet* 344:1105–1110 (1994)). But until the present invention, there has been no suggestion of treatment of autoimmune disease with anti-IFNγ antibodies, nor with a combination of anti-cytokine antibodies. Nor have the effects of such treatments been evaluated in clinical trials. Given the striking long-term results produced by the present method, the combined anti-cytokines, e.g., anti-TNFα antibodies in conjunction with anti-IFNγ antibodies, may even act synergistically.

Example 5

Treatment of Patients with Systemic Lupus Erythematosus

Human patients with systemic lupus erythematosus (SLE) were selected after obtaining approval and informed consent, in much the same manner as set forth in Example 3, and divided into two groups consisting of at least four (4) patients each. The basis for selection was the patient's failure to respond to conventional therapy for SLE. Using polyclonal anti-IFNγ antibodies and anti-TNF antibodies in accordance with Example 3, one group of patients was treated with anti-IFNγ antibodies, while the other group was treated with anti-IFNγ antibodies and anti-TNF antibodies. The antibodies were administered in accordance with the schedule and amounts set forth in Example 3 for 5 consecutive days.

Preliminary results, based upon at least one patient in each group, indicate that pain and swelling in joints have decreased and skin lesions have disappeared, further indicating that a common mechanism underlies all autoimmune disease, with disturbed cytokine production in different target cells producing the various clinical manifestations.

Comparable results are achieved by extracorporeal immunosorption as defined above, or by extracorporeal immunosorption in conjunction with administration of an autoimmune inhibitor.

Example 6

Treatment of Patients with Multiple Sclerosis

Human patients with multiple sclerosis (MS) were selected after obtaining approval and informed consent, in much the same manner as set forth in Example 3, and divided into three groups consisting of at least five (5) patients each. The basis for selection was the presence of active MS and the patient's failure to respond to conventional therapy for MS. Using polyclonal anti-IFNγ antibodies and anti-TNF antibodies in accordance with Example 3, one group of patients was treated with anti-IFNγ antibodies, one group with anti-TNF antibodies, and one group with anti-IFNγ antibodies and anti-TNF antibodies. The antibodies were administered in accordance with the schedule and amounts set forth in Example 3 for 5 consecutive days, and the patients were followed for at least two and one half (2 ½) months.

Results of the treatment were evaluated in terms of measured neurological deficiencies and general patient function at the end of the 2½-month period, as compared with pretreatment determinations of the same criteria. Determinations were based upon the Disability Status Scale (DSS) devised by J. F. Kurztke, and the Functional System Scale (FSS), respectively. Decreasing numbers indicate improvement on the DSS scale, while increasing numbers indicate improvement on the FSS scale. Preliminary results indicate that improvement was most evident in the group treated with anti-IFNγ antibodies and in the group treated with anti-IFNγ antibodies and anti-TNF antibodies, as determined by the two scales.

Additional studies indicate that the treatment may be further enhanced by the administration of beta interferon (IFNβ). When eight million international units (IU) of IFNβ were given subcutaneously to patients every other day for two years, there was a decrease in the rate of exacerbated symptoms in some patients. Consequently, an optimal treatment of an MS patient appears to be the use of anti-IFNγ antibodies or a combination of anti-IFNγ antibodies and